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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/674,857	11/07/2000	Kathryn Armour	620-117	5675

23117 7590 04/25/2005

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EXAMINER	
HUYNH, PHUONG N	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 04/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/674,857	ARMOUR ET AL.	
	Examiner	Art Unit	
	Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 December 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-29,31-33,37-42 and 46-67* is/are pending in the application.

4a) Of the above claim(s) *31* is/are withdrawn from consideration.

5)☒ Claim(s) *16-27,32,37-39,41,46-48,51,55,56 and 64-67* is/are allowed.

6)☒ Claim(s) *28-29, 33, 40, 42, 49-50, 52-54, 57 and 62-63* is/are rejected.

7)☒ Claim(s) *58-61* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 16-29, 31-33, 37-42 and 46-67 are pending.

2. The following new grounds of rejections are necessitated by the amendment filed 12/30/04.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 28-29, 33, 40, 42, 49-50, 52-54, 57 and 62-63 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for (1) a binding molecule as set forth in claims 32, 37-39, 41, 46-48, and 64-65, (2) an isolated nucleic acid consisting of a nucleotide sequence encoding the effector domain of the said binding molecule, (3) an isolated nucleic comprising a nucleotide sequence encoding the binding molecule as set forth in claim 51-53, (4) a host comprising or transformed with said vector, (5) a process of producing said binding molecule as set forth in claims 55-56, and 66-67 and (6) a method of binding a target molecule to the FcγRIIb using said binding molecule, **does not** reasonably provide enablement for (1) any pharmaceutical composition as set forth in claims 40, and 49 (2) any binding molecule wherein the chimeric CH2 "comprises" G1Δab (SEQ ID NO: 1), G2Δa (SEQ ID NO: 2) as set forth in claims 33 and 42, (3) a method of treating a patient for any disorder selected from Graft-vs-host disease, host-vs-graft disease, organ transplant rejection, bone-marrow transplant rejection, autoimmunity such as vasculitis, autoimmune haemolytic anaemia, autoimmune thrombocytopenia and arthritis; alloimmunity such as foetal/neonatal alloimmune thrombocytopenia; asthma and allergy, chronic or acute inflammatory diseases such as Chrohn's; IIDN; Goodpastures, sickle cell anaemia, coronary artery occlusion (claims 57-58 and 62-63) by administering to a patient a binding molecule as set forth in claim 41, and (4) an isolated nucleic acid "comprising" of a nucleotide sequence encoding the effector domain of the said binding molecule. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification discloses only a binding molecule which is a recombinant polypeptide comprising" (i) a binding domain capable of binding to a target molecule such as the ones recited in claim 39, and (ii) an effector domain having an amino acid sequence homologous to a constant domain of a human immunoglobulin heavy chain; wherein the binding molecule is capable of binding the target molecule without triggering significant complement dependent lysis, or cell mediated destruction of the target, and the effector domain is capable of specifically binding FcyRIIb and optionally FcRn, and wherein the effector domain is comprises a chimeric CH2 domain which is derived from two or more human immunoglobulin heavy chain CH2 domains, which human immunoglobulins are selected from IgG1, IgG2 and IgG4, and wherein the effector domain has a reduced affinity for FcγR1, FcγRIIa and FcγRIII and a reduced ability to mediate complement lysis by comparison with said constant domain of a human immunoglobulin heavy chain and wherein the chimeric CH2 domain is a human immunoglobulin heavy chain CH2 domain which has the following blocks of amino acids at the stated positions: 233P, 234V, 235A, no residue at 236, 327G, 330S and 331S numbered with respect to the EU system of Kabat and is at least 98% identical to a CH2 sequence (residues 231-340) from human IgG1 or IgG2 having said modified amino acids. The specification further discloses a binding molecule which is a recombinant polypeptide comprising" (i) a binding domain capable of binding to a target molecule such as the ones recited in claim 39, and (ii) an effector domain having an amino acid sequence homologous to a constant domain of a human immunoglobulin heavy chain; wherein the binding molecule is capable of binding the target molecule without triggering significant complement dependent lysis, or cell mediated destruction of the target, and the effector domain is capable of specifically binding FcyRIIb and optionally FcRn, and wherein the effector domain is comprises a chimeric CH2 domain which is derived from two or more human immunoglobulin heavy chain CH2 domains, which human immunoglobulins are selected from IgG1, IgG2 and

IgG4, and wherein the effector domain has a reduced affinity for FcγR1, FcγRIIa and FcγRIII and a reduced ability to mediate complement lysis by comparison with said constant domain of a human immunoglobulin heavy chain and wherein the chimeric CH2 domain is a human immunoglobulin heavy chain CH2 domain which has the following blocks of amino acids at the stated positions: 233P, 234V, 235A, 236G, 327G, 330S and 331S numbered with respect to the EU system of Kabat and is at least 98% identical to a CH2 sequence (residues 231-340) from human IgG1 or IgG4 having said modified amino acids.

The specification does not teach how to use any pharmaceutical composition mentioned above because there is a lack of guidance as to the binding specificity of the *binding domain* of the claimed binding molecule for a pharmaceutical composition for treating any and all disorder commensurate in scope with these claims. Applicant has not provided any biochemical information (e.g. molecular weight, amino acid composition, N-terminal sequence, etc.) of the "target molecule" from all disease, let alone the generic binding molecule can treat any and all diseases. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. Given the unlimited number of target molecule to which the binding molecule binds, there is a lack of in vivo working example demonstrating the efficacy of all binding molecule without knowing the target molecule to which the binding molecule binds for treating any and all diseases such as Graft-vs-host disease, host-vs-graft disease, organ transplant rejection, bone-marrow transplant rejection, autoimmunity such as vasculitis, autoimmune haemolytic anaemia, autoimmune thrombocytopenia and arthritis; alloimmunity such as foetal/neonatal alloimmune thrombocytopenia; asthma and allergy, chronic or acute inflammatory diseases such as Chrohn's; IIDN; Goodpastures, sickle cell anaemia, and coronary artery occlusion. Until the target molecule in the particular disease has been identified and then the binding molecule can be made, the specification as filed merely extends an invitation to one skill in the art for further experimentation to arrive at the claimed invention. Since treating autoimmune disease can be species- and model-dependent, it is not clear that reliance on in vitro binding accurately reflects on the efficacy of the claimed binding molecule. A pharmaceutical composition in the absence of in vivo data is unpredictable for the following reasons: (1) given the generic nature of the binding molecule in the claimed pharmaceutical composition, the binding specificity of the claimed binding molecule in the particular disorder is non-specific. (2) the art and the specification do not teach binding molecule such as antibody to CAMPATH-1, RhD, CD3 GBM collagen, integrin, HPA alloantigen or neutrophil antigen having the claimed

effector domain can treat allergy, for example. (3) Likewise, the art and the specification do not teach binding molecule such as antibody to Der P1 having the claimed effector domain can treat Graft-vs-host disease, host-vs-graft disease, autoimmune haemolytic anemia, thrombocytopenia, Chrohn's disease, HDN, Goodpasture, sickle cell anaemia and coronary artery occlusion, for example.

With regard to claims 33 and 42, the term "comprises" is open-ended. It expands the chimeric CH2 domain, which is a fragment of the constant region of the antibody, to include additional amino acids at either or both ends. There is a lack of guidance as to which undisclosed amino acids to be added and whether the resulting binding molecule maintains its structure and achieves the desire functions. The same reasoning applies to claim 50.

Again, the term "comprising" is open-ended. It expands the effector domain, which is a fragment of the binding molecule to include additional nucleotides at either or both ends. There is a lack of guidance as to which nucleotides to be added and whether the resulting polynucleotide encodes an effector domain that maintains its structure and achieves the desired functions. Since the polynucleotide in claim 50 is not enabled, it follows that the vector (claim 52) and host cell (claim53) are not enabled.

For these reasons, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

Note, deleting "pharmaceutical" in claims 40, and 49 would obviate this rejection since one skill in the art know how to use a preparation comprising the claimed binding molecule binding molecule and a pharmaceutical acceptable carrier to bind FcγRIIb.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

6. Claims 57 and 62 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The preamble "a method of binding a molecule" in claim 57 is ambiguous and indefinite because the target molecule in the claimed binding molecule is not defined. One of ordinary skill in the art cannot appraise the metes and bound of the claimed invention.

The "method of claim 58 for treatment of a patient" in claim 62 is ambiguous because the method in claim 58 is for binding a target molecule to FcγRIIb, not treatment of disease as claim.

7. Claims 16-27, 32, 37-39, 41, 46-48, 51, 55-56, and 64-67 are allowed.

8. Claims 58-61 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh "NEON" whose telephone number is (571) 272-0846. The examiner can normally be reached Monday through Friday from 9:00 am to 5:30 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone

are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The IFW official Fax number is (571) 273-8300.

11. Any information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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April 15, 2005

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